Rett syndrome

Rett syndrome is a brain disorder that occurs almost exclusively in girls. The most common form of the condition is known as classic Rett syndrome. After birth, girls with classic Rett syndrome have 6 to 18 months of apparently normal development before developing severe problems with language and communication, learning, coordination, and other brain functions. Early in childhood, affected girls lose purposeful use of their hands and begin making repeated hand wringing, washing, or clapping motions. They tend to grow more slowly than other children and have a small head size (microcephaly). Other signs and symptoms that can develop include breathing abnormalities, seizures, an abnormal side-to-side curvature of the spine (scoliosis), and sleep disturbances.

Researchers have described several variant or atypical forms of Rett syndrome, which can be milder or more severe than the classic form.

Frequency

This condition affects an estimated 1 in 8,500 females.

Genetic Changes

Classic Rett syndrome and some variant forms of the condition are caused by mutations in the *MECP2* gene. This gene provides instructions for making a protein (MeCP2) that is critical for normal brain function. Although the exact function of the MeCP2 protein is unclear, it is likely involved in maintaining connections (synapses) between nerve cells (neurons). It may also be necessary for the normal function of other types of brain cells.

The MeCP2 protein is thought to help regulate the activity of genes in the brain. This protein may also control the production of different versions of certain proteins in brain cells. Mutations in the *MECP2* gene alter the MeCP2 protein or result in the production of less protein, which appears to disrupt the normal function of neurons and other cells in the brain. Specifically, studies suggest that changes in the MeCP2 protein may reduce the activity of certain neurons and impair their ability to communicate with one another. It is unclear how these changes lead to the specific features of Rett syndrome.

Several conditions with signs and symptoms overlapping those of Rett syndrome have been found to result from mutations in other genes. These conditions, including *FOXG1* syndrome, were previously thought to be variant forms of Rett syndrome. However, doctors and researchers have identified some important differences between the conditions, so they are now usually considered to be separate disorders.

Inheritance Pattern

In more than 99 percent of people with Rett syndrome, there is no history of the disorder in their family. Many of these cases result from new mutations in the *MECP2* gene.

A few families with more than one affected family member have been described. These cases helped researchers determine that classic Rett syndrome and variants caused by *MECP2* gene mutations have an X-linked dominant pattern of inheritance. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes. The inheritance is dominant if one copy of the altered gene in each cell is sufficient to cause the condition.

Males with mutations in the *MECP2* gene often die in infancy. However, a small number of males with a genetic change involving *MECP2* have developed signs and symptoms similar to those of Rett syndrome, including intellectual disability, seizures, and movement problems. In males, this condition is described as *MECP2*-related severe neonatal encephalopathy.

Other Names for This Condition

- autism-dementia-ataxia-loss of purposeful hand use syndrome
- Rett disorder
- Rett's disorder
- Rett's syndrome
- RTS
- RTT

Diagnosis & Management

These resources address the diagnosis or management of Rett syndrome:

- Boston Children's Hospital
  http://www.childrenshospital.org/conditions-and-treatments/conditions/rett-syndrome
- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/rett-syndrome
- GeneReview: MECP2-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1497
- Genetic Testing Registry: Rett syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0035372/

- MedlinePlus Encyclopedia: Rett Syndrome
  https://medlineplus.gov/ency/article/001536.htm
- RettSyndrome.org: Rett Syndrome Clinics
  http://www.rettsyndrome.org/for-families/clinics

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Rett Syndrome
  https://medlineplus.gov/ency/article/001536.htm
- Health Topic: Rett Syndrome
  https://medlineplus.gov/rettsyndrome.html

Genetic and Rare Diseases Information Center

- Atypical Rett syndrome
  https://rarediseases.info.nih.gov/diseases/4694/atypical-rett-syndrome
- Rett syndrome
  https://rarediseases.info.nih.gov/diseases/5696/rett-syndrome

Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health & Human Development
  https://www.nichd.nih.gov/health/topics/rett/Pages/default.aspx
- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Rett-Syndrome-Information-Page

Educational Resources

- Disease InfoSearch: Rett syndrome
  http://www.diseaseinfosearch.org/Rett+syndrome/6294
- InterRett: International Rett Syndrome Database
  http://www.aussierett.org.au/participate-in-research/interrett.aspx
- Kennedy Krieger Institute
  https://www.kennedykrieger.org/patient-care/diagnoses-disorders/rett-syndrome
- MalaCards: rett syndrome
  http://www.malacards.org/card/rett_syndrome
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Rett%20syndrome&type=profile
- Orphanet: Rett syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=778
- Swedish Information Center for Rare Diseases
  http://www.socialstyrelsen.se/rarediseases/rettsyndrome

Patient Support and Advocacy Resources

- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/rett-syndrome/
- RareConnect
  https://www.rareconnect.org/en/community/rett-syndrome
- Resource List from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/rett_syn.html
- Rett Syndrome Association UK
  http://www.rettuk.org/
- Rett Syndrome Research Trust
  http://reverserett.org/
- RettSyndrome.org
  https://www.rettsyndrome.org/

GeneReviews

- MECP2-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1497

Genetic Testing Registry

- Rett syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0035372/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Rett+syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Rett+Syndrome%5BMAJR%5D%29+AND+%28Rett+syndrome%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D

OMIM

- RETT SYNDROME
  http://omim.org/entry/312750

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